General

Guideline Title

Congress of Neurological Surgeons systematic review and evidence-based guideline on posttreatment follow-up evaluation of patients with nonfunctioning pituitary adenomas.

Bibliographic Source(s)

Ziu M, Dunn IF, Hess C, Fleseriu M, Bodach ME, Tumialan LM, Oyesiku NM, Patel KS, Wang R, Carter BS, Chen JY, Chen CC, Patil CG, Litvack Z, Zada G, Aghi MK. Congress of Neurological Surgeons systematic review and evidence-based guideline on posttreatment follow-up evaluation of patients with nonfunctioning pituitary adenomas. Neurosurgery. 2016 Oct;79(4):E541-3. [23 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

The rating schemes used for the strength of the evidence (Class I-III) and the levels of recommendations (Level I-III) are defined at the end of the "Major Recommendations" field.

Question

What is the optimal protocol for posttreatment imaging of nonfunctioning pituitary adenoma (NFPA) patients?

Target Population

These recommendations apply to adult patients with recurrent or residual NFPAs.

Level III Recommendations

> The use of magnetic resonance imaging (MRI) with the addition of T2 and T1 weighted images with fat suppression sequences is recommended for radiologic follow-up of NFPAs after surgical or radiation treatment.
> Long-term radiologic surveillance monitoring after surgical or radiation therapy treatment of NFPAs to evaluate for tumor recurrence or regrowth is recommended. There is insufficient evidence to make a

recommendation on the length of time of surveillance.
It is recommended that patients who undergo radiologically proven gross total resection of the NFPA be followed less frequently than those undergoing subtotal resection.
It is recommended that the first radiologic study to evaluate the extent of resection of the NFPA be performed 3 to 4 months after surgical intervention.

Level Inconclusive Recommendations

There is insufficient evidence to make a recommendation regarding the frequency of radiologic surveillance follow-up after surgical or radiation treatment of patients with NFPAs.
There is insufficient evidence to make a recommendation regarding the timing of initial radiologic follow-up after radiation therapy.

Question

What is the optimal protocol for posttreatment endocrine evaluation of NFPA patients?

Target Population

These recommendations apply to adult patients with recurrent or residual NFPAs.

Level III Recommendations

Endocrine evaluation for pituitary dysfunction is recommended after surgery and/or radiation therapy in patients with NFPAs.
Postoperative evaluation of adrenal function on postoperative day 2, 6 weeks, and then 12 months after treatment is recommended to determine adrenal function in patients with NFPAs.
Corticosteroid supplementation in the perioperative period is recommended for NFPA patients with preoperative or immediate postoperative (day 2) hypocortisolemia.
Postoperative endocrinologic follow-up in patients with normal pituitary function beyond 1 year is not recommended, as it does not offer any further benefit.
Indefinite endocrinologic follow-up is recommended in all patients with abnormal pituitary function who undergo surgical resection of NFPAs.
Indefinite endocrine follow-up is recommended in patients who undergo radiation therapy for NFPAs for serial surveillance of their pituitary function.
Surveillance of serum sodium levels on the first 2 days after surgery and on postoperative days 7 and 8 is recommended to prevent symptomatic postoperative hyponatremia.

Level Inconclusive Recommendations

There is insufficient evidence to make a recommendation on the detection and treatment of postoperative diabetes insipidus (DI).
There is insufficient evidence to make a recommendation regarding the frequency of endocrinologic follow-up evaluation after surgery or radiation therapy.

Question

What is the optimal protocol for posttreatment ophthalmologic evaluation in NFPA patients?

Target Population

These recommendations apply to adult patients with recurrent or residual NFPAs.

Level III Recommendation

Postoperative ophthalmologic follow-up in patients undergoing surgical and/or radiation therapy treatment for NFPAs is recommended to evaluate the change in visual field and visual acuity postoperatively. There is insufficient evidence to make a recommendation on the length of time for this surveillance and the frequency.

Question

What is the role for combined posttreatment follow-up (integrated imaging, ophthalmologic, and endocrine evaluation) in NFPA patients?

Target Population

These recommendations apply to adult patients with recurrent or residual NFPAs.

Level Inconclusive Recommendation

There is insufficient evidence to make a recommendation on how to integrate radiologic, ophthalmologic, and endocrinologic follow-up after surgical resection or radiation treatment of patients with NFPAs.

Definitions

Evidence Classification for Clinical Assessment Studies

Class I	Evidence provided by one or more well-designed clinical studies in which interobserver and/or intraobserver reliability is represented by a Kappa statistic ≥0.60. The Kappa statistic is defined as (po-pe)/(1-pe) where po is the relative observed agreement and pe is the hypothetical probability of chance agreement.
Class II	Evidence provided by one or more well-designed clinical studies in which interobserver and/or intraobserver reliability is represented by a Kappa statistic ≥0.40
Class III	Evidence provided by one or more well-designed clinical studies in which interobserver and/or intraobserver reliability is represented by a Kappa statistic <0.40

Strength of Recommendations Rating Scheme

Level I: High degree of clinical certainty (Class I evidence or overwhelming Class II evidence)

Level II: Clinical certainty (Class II evidence or a strong consensus of Class III evidence)

Level III: Clinical uncertainty (inconclusive or conflicting evidence or opinion)

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Nonfunctioning pituitary adenomas (NFPAs)

Guideline Category

Evaluation

Management

Clinical Specialty

Endocrinology

Neurological Surgery

Neurology

Oncology

Ophthalmology

Radiation Oncology

Radiology

Intended Users

Physicians

Guideline Objective(s)

- To create evidence-based guidelines in an attempt to formulate guidance for posttreatment follow-up of patients with nonfunctioning pituitary adenomas (NFPAs) in a consistent, rigorous, and cost-effective way
- To address issues such as the need for radiologic, endocrinologic, and ophthalmologic posttreatment follow-up, the frequency of which these specific surveillance modalities should be performed, and the length of time
- To address the question whether there is a need for corticosteroid administration to these patients and the frequency of monitoring for any electrolyte imbalance

Target Population

Adult patients with recurrent or residual nonfunctioning pituitary adenoma (NFPA)

Interventions and Practices Considered

1. Posttreatment radiologic follow-up
    - Magnetic resonance imaging (MRI) with the addition of T2 and T1 weighted images with fat suppression sequence
    - Long-term radiologic surveillance monitoring to evaluate for recurrence
2. Posttreatment endocrinologic follow-up
    - Endocrine evaluation for pituitary dysfunction
    - Postoperative evaluation of adrenal function
    - Corticosteroid supplementation
    - Indefinite endocrinologic follow-up
    - Surveillance of serum sodium
3. Posttreatment ophthalmologic follow-up (insufficient evidence for recommendation on length and frequency of these follow-ups)

Note: The following were considered but not recommended due to insufficient evidence: specific frequency and timing of radiologic surveillance; detection and treatment of postoperative diabetes insipidus; frequency of endocrinologic follow-up; combined post-treatment follow-up (integrated imaging, ophthalmologic, and endocrine evaluation).

Major Outcomes Considered

- Residual tumor rate
- Residual tumor regrowth

- Tumor recurrence rate
- Interval and duration of radiologic, endocrinologic, and ophthalmologic follow-up
- Regrowth-free survival rates at 5 and 10 years
- Pituitary function
- Serum cortisol levels
- Changes in visual field/visual acuity

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

General Search Strategy

Literature Search

The guideline task force collaborated with a medical librarian to search for articles published from January 1, 1966, to October 1, 2014. Searches were conducted in two electronic databases, PubMed and The Cochrane Central Register of Controlled Trials. Strategies for searching electronic databases were constructed by the guideline task force members and medical/research librarians using previously published search strategies to identify relevant studies. The root search strategies are provided in Appendix A of the introduction and methodology companion and the chapter-specific search strategies are provided in the appendix of the full version of the guideline (see the "Availability of Companion Documents" field).

The searches of electronic databases were supplemented with manual screening of the bibliographies of all retrieved publications. The bibliographies of recent systematic reviews and other review articles for potentially relevant citations were also screened. All articles identified were subject to the study selection criteria listed below. The guideline task force also examines lists of included and excluded studies for errors and omissions.

Article Inclusion Criteria

Articles were retrieved and included only if they met specific inclusion criteria. These criteria were also applied to articles provided by the evidence-based clinical practice guideline task force members who supplemented the electronic database searches with manual searches of the bibliographies. To reduce bias, these criteria were specified *a priori* before conducting the literature searches. For the purposes of this guideline, articles had to meet the following criteria to be included as evidence to support the recommendations presented in this guideline:

Investigated patients suspected of having a pituitary mass
Enrolled patients ≥18 years of age
Either enrolled exclusively nonfunctioning pituitary adenoma (NFPA) patients OR combined the results of patients with NFPAs and functioning pituitary adenomas and/or other pituitary masses with ≥90% of the patients having NFPAs
Was a full article report of a clinical study
If a prospective case series, reported baseline values
Appeared in a peer-reviewed publication

Enrolled ≥10 NFPA patients per arm per intervention (20 total) for each outcome
Was of humans
Was published in or after 1966
Quantitatively presented results

Article Exclusion Criteria

Articles of the following types were excluded as evidence to support the recommendations presented in this guideline:

In vitro studies
Studies performed on cadavers
Studies not published in English
Medical records reviews, meeting abstracts, historical articles, editorial, letters, or commentaries
Systematic reviews, meta-analyses, or guidelines developed by others

Specific Methods for This Guideline

Results

After an extensive search on PubMed and the Cochrane Central Register of Controlled Trials databases, 579 articles were located. The duplicates from the search in different databases were eliminated. By reviewing the titles and/or abstracts, reviewers excluded all articles referring to functioning pituitary adenomas and/or other sellar and parasellar pathologies and those discussing exclusively evaluation, treatment, and follow-up in patients younger than 18 years of age. They excluded as well those publications that discussed exclusively treatment options and outcomes and those discussing diagnostic methodologies before the beginning of any type of treatment. Additionally, they excluded all articles discussing experimental therapy in animal tumor models. The remaining 114 articles underwent full text review. Only 23 articles met all of the inclusion criteria and were used in formulating these evidence-based clinical guidelines. The majority of the remaining 114 articles that underwent full review were excluded because they reported only postoperative outcomes or reported long-term follow-up methods in all types of pituitary tumors with results that were not separable between NFPAs and functioning pituitary adenomas (FPAs), and the remainder because they lacked significance for the topic.

Number of Source Documents

Only 23 articles met all of the inclusion criteria and were used in formulating these evidence-based clinical guidelines.

See Figure 1 in the full version of the guideline for the flowchart summarizing study selection (see the "Availability of Companion Documents" field).

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Evidence Classification for Clinical Assessment Studies

Class I	Evidence provided by one or more well-designed clinical studies in which interobserver and/or intraobserver reliability is represented by a Kappa statistic ≥0.60. The Kappa statistic is defined as (po-pe)/(1-pe) where po is the relative observed agreement and pe is the hypothetical probability of chance agreement.
Class	Evidence provided by one or more well-designed clinical studies in which interobserver and/or

II	intraobserver reliability is represented by a Kappa statistic ≥0.40
Class III	Evidence provided by one or more well-designed clinical studies in which interobserver and/or intraobserver reliability is represented by a Kappa statistic <0.40

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Rating the Quality of the Evidence and Levels of Recommendations

The quality and classification of evidence (see the "Rating Scheme for the Strength of the Evidence" field) was rated using an evidence hierarchy developed by the American Association of Neurological Surgeons/Congress of Neurological Surgeons (AANS/CNS) Guidelines Committee for each of four different study types: therapeutic, prognostic, diagnostic, and economic or decision modeling. The methodology used to conduct quality evaluations of the evidence can be located on the CNS Web site (see also the "Availability of Companion Documents" field). The level/strength of recommendation (i.e., Level I, II, or III) was linked to the quality of the overall body of evidence included in the chapter and in support of a given recommendation.

Methods Used to Formulate the Recommendations

Expert Consensus (Nominal Group Technique)

Description of Methods Used to Formulate the Recommendations

Process Overview

A multidisciplinary task force comprised of physician volunteers and evidence-based medicine trained methodologists conducted a systematic review of the literature relevant to the management of non-functioning pituitary adenomas (NFPAs). The physician volunteers represented neurosurgeons, neuro-ophthalmologists, neuroradiologists, and endocrinologists with expertise in pituitary adenomas. The evidence-based medicine trained methodologists had previous experience in guidelines production for the Joint Guidelines Committee (JGC) of the Congress of Neurological Surgeons (CNS) and the American Association of Neurological Surgeons (AANS). During the development process, the task force participated in a series of conference calls and meetings. Multiple iterations of written review were conducted by the individuals of the panel and various CNS/AANS Committees prior to approval.

Guideline Task Force Panel Consensus

The guideline task force panel included context experts from multiple disciplines and various areas of therapy to address the topics addressed in this guideline. Sub-task force members were assigned to a specific chapter and were involved in the literature review, the creation and editing of the evidence tables, reviewing and voting of the final recommendations.

Voting on the Recommendations

The task force used a structured voting technique to finalize and approve the final recommendations, language, and strength of recommendations, presented in this review. The voting technique is referred to as the nominal group technique. This technique includes up to three rounds of voting, using secret ballots to ensure task force members are blinded to the responses of other task force members. All the recommendations in this review were approved following the first round of voting and no further discussion was needed to finalize the recommendations. During the course of editing and finalization of

the document, changes were made to allow recommendations to conform to the rules of evidence and language as described above. When this occurred, the changes were reviewed and approved by the group.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations Rating Scheme

Level I: High degree of clinical certainty (Class I evidence or overwhelming Class II evidence)

Level II: Clinical certainty (Class II evidence or a strong consensus of Class III evidence)

Level III: Clinical uncertainty (inconclusive or conflicting evidence or opinion)

Cost Analysis

The guideline authors reviewed published cost analyses.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Guideline Approval Process

The guideline draft was circulated to the entire task force for final review and approval prior to submission for peer review by the Joint Guidelines Committee (JGC) of the Congress of Neurological Surgeons (CNS) and the American Association of Neurological Surgeons (AANS). Due to the reviewers' knowledge of evidence-based medicine and clinical practice guidelines methodology training, the JGC peer reviewers served as the journal's editorial reviewers. As a part of the JGC review process, the reviewers provided input on the content of the guideline and suggested revisions prior to approval and endorsement of the draft guideline by the CNS and AANS prior to publication. The development of this guideline was editorially independent from the funding agencies (CNS Executive Committee, and AANS/CNS Joint Tumor Section Executive Committee), the CNS and Joint Tumor Section.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

All studies were all classified as Class III evidence.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

All considered, there is Class III evidence that radiologic follow-up remains the best method to evaluate the tumor for regrowth or recurrence after surgery and radiation therapy (RT) and avoid recurrence of endocrinologic dysfunction and visual disturbances.

Potential Harms

Unrecognized adrenocorticotrophic hormonal deficiency in the postoperative period can cause fatigue, anorexia, nausea, vomiting, hypotension, fever, metabolic changes, and rarely death. In response, different institutions have implemented disparate strategies; in some centers, supplemental corticosteroids are given to all patients for several weeks before the hypothalamic-pituitary-adrenal axis function is tested, while others have advocated testing the adrenal axis after surgery and deciding on the use of corticosteroid supplementation only if a dysfunction is found. This later approach has the advantage of reducing the side effects to the patients deriving from supplemental steroids and reducing healthcare costs, yet with the risk of undertreating deficiency in some cases.

Qualifying Statements

Qualifying Statements

Disclaimer of Liability

This clinical systematic review and evidence-based guideline was developed by a physician volunteer task force as an educational tool that reflects the current state of knowledge at the time of completion. The presentations are designed to provide an accurate review of the subject matter covered. This guideline is disseminated with the understanding that the recommendations by the authors and consultants who have collaborated in its development are not meant to replace the individualized care and treatment advice from a patient's physician(s). If medical advice or assistance is required, the services of a physician should be sought. The recommendations contained in this guideline may not be suitable for use in all circumstances. The choice to implement any particular recommendation contained in this guideline must be made by a managing physician in light of the situation in each particular patient and on the basis of existing resources.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Mobile Device Resources

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Ziu M, Dunn IF, Hess C, Fleseriu M, Bodach ME, Tumialan LM, Oyesiku NM, Patel KS, Wang R, Carter BS, Chen JY, Chen CC, Patil CG, Litvack Z, Zada G, Aghi MK. Congress of Neurological Surgeons systematic review and evidence-based guideline on posttreatment follow-up evaluation of patients with nonfunctioning pituitary adenomas. Neurosurgery. 2016 Oct;79(4):E541-3. [23 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 Oct

Guideline Developer(s)

Congress of Neurological Surgeons - Professional Association

Source(s) of Funding

These evidence-based clinical practice guidelines were funded exclusively by the Congress of Neurological Surgeons and the Tumor Section of the Congress of Neurological Surgeons and the American Association of Neurological Surgeons, which received no funding from outside commercial sources to support the development of this document.

Guideline Committee

Nonfunctioning Pituitary Adenoma Guideline Task Force

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Potential Conflicts of Interest

All nonfunctioning pituitary adenoma (NFPA) Guideline Task Force members were required to disclose all potential conflicts of interest (COIs) prior to beginning work on the guideline, using the COI disclosure form of the American Association of Neurological Surgeons/Congress of Neurological Surgeons (AANS/CNS) Joint Guidelines Committee. The CNS Guidelines Committee and Guideline Task Force Chair reviewed the disclosures and either approved or disapproved the nomination and participation on the task force. The CNS Guidelines Committee and Guideline Task Force Chair may approve nominations of Task Force Members with possible conflicts and restrict the writing, reviewing and/or voting privileges of that person to topics that are unrelated to the possible COIs.

Disclosures

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

Guideline Endorser(s)

American Association of Neurological Surgeons - Medical Specialty Society

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the Neurosurgery Web site . Also available in ePub format from the Neurosurgery Web site .

Availability of Companion Documents

The following are available:

Ziu M, Dunn IF, Hess C, Fleseriu M, Bodach ME, Tumialan LM, Oyesiku NM, Patel KS, Wang R, Carter BS, Chen JY, Chen CC, Patil CG, Litvack Z, Zada G, Aghi MK. Congress of Neurological Surgeons systematic review and evidence-based guideline on posttreatment follow-up evaluation of patients with nonfunctioning pituitary adenomas. Full guideline. Schaumburg (IL): Congress of Neurological Surgeons (CNS); 2016 Oct. 54 p. Available from the Congress of Neurological Surgeons (CNS) Web site .

Aghi MK, Chen CC, Fleseriu M, Newman SA, Lucas JW, Kuo JS, Barkhoudarian G, Farrell CJ, Sheehan J, Ziu M, Dunn IF. Congress of Neurological Surgeons systematic review and evidence-based guidelines on the management of patients with nonfunctioning pituitary adenomas: executive summary. Neurosurgery. 2016 Oct;79(4):521-3. Available from the Neurosurgery Web site .

Aghi MK, Bodach ME, Tumialan LM, Oyesiku NM, Patil CG, Litvack Z, Zada G. Congress of Neurological Surgeons systematic review and evidence-based guidelines on the management of patients with nonfunctioning pituitary adenomas: introduction and methodology. Schaumburg (IL): Congress of Neurological Surgeons (CNS); 2016 Oct. 12 p. Available from the CNS Web site .

Congress of Neurological Surgeons (CNS). Guideline development methodology: endorsed by the American Association of Neurological Surgeons (AANS), the Congress of Neurological Surgeons (CNS), and the AANS/CNS Joint Guideline Committee. Schaumburg (IL): Congress of Neurological Surgeons (CNS); 2012 Feb. 12 p. Available from the CNS Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on February 10, 2017. The information was verified by the guideline developer on February 22, 2017.

Copyright Statement

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